

FILE 'USPAT' ENTERED AT 21:12:30 ON 12 SEP 1997

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\* WELCOME TO THE \*  
\* U. S. PATENT TEXT FILE \*  
\*\*\*\*\*

=> s ((tumor? or tumour?)(w)necro? factor?)(5a)receptor?

19357 TUMOR?

1789 TUMOUR?

8023 NECRO?

390714 FACTOR?

1684 NECRO? FACTOR?

(NECRO?(W)FACTOR?)

28325 RECEPTOR?

L1 73 ((TUMOR? OR TUMOUR?)(W)NECRO?

FACTOR?)(5A)RECEPTOR?

=> s l1 and (dna? or cdna? or rna? or mrna? or clon?)

20738 DNA?

6513 CDNA?

11909 RNA?

5858 MRNA?

17106 CLON?

L2 70 L1 AND (DNA? OR CDNA? OR RNA? OR MRNA?  
OR CLON?)

=> d 1-20

1. 5,665,859, Sep. 9, 1997, Molecules influencing the shedding of the TNF receptor, their preparation and their use; David Wallach, et al., 530/328; 435/69.2, 226; 530/327, 350 :IMAGE AVAILABLE:

2. 5,663,070, Sep. 2, 1997, Recombinant production of a soluble splice variant of the Fas (Apo-1) antigen, fas TM; Philip J. Barr, et al., 435/325, 69.1, 253.3, 254.11, 320.1, 348, 358, 361; 536/23.5 :IMAGE AVAILABLE:

3. 5,661,004, Aug. 26, 1997, Lymphotoxin-.beta., lymphotoxin-.beta. complexes, pharmaceutical preparations and therapeutic uses thereof; Jeffrey Browning, et al., 435/69.1; 536/23.5 :IMAGE AVAILABLE:

4. 5,658,949, Aug. 19, 1997, Inhibition of tumor necrosis factor by retinoic acid; Bharat B. Aggarwal, 514/557, 825, 895, 903 :IMAGE AVAILABLE:

5. 5,654,407, Aug. 5, 1997, Human anti-TNF antibodies; Petra Boyle, et al., 530/388.15; 424/142.1, 145.1, 158.1; 435/335; 530/388.23, 388.24 :IMAGE AVAILABLE:

6. 5,652,353, Jul. 29, 1997, \*\*DNAs\*\* encoding tumor necrosis factor-.alpha. muteins; Walter Fiers, et al., 536/23.5; 435/69.5, 172.3, 252.3, 320.1; 935/11, 22, 70, 73 :IMAGE AVAILABLE:

7. 5,652,225, Jul. 29, 1997, Methods and products for nucleic acid delivery; Jeffrey M. Isner, 514/44; 424/93.2; 435/172.1, 172.3, 320.1; 536/23.5, 23.51; 604/51, 52, 53; 935/9, 22, 32, 33, 34, 52, 57 :IMAGE AVAILABLE:

8. 5,652,210, Jul. 29, 1997, Soluble splice variant of the Fas (APO-1)

antigen, Fas.DELTA.TM; Philip J. Barr, et al., 514/2; 435/69.1; 514/8; 530/350, 395 :IMAGE AVAILABLE:

9. 5,650,316, Jul. 22, 1997, Uses of triplex forming oligonucleotides for the treatment of human diseases; Bharat B. Aggarwal, et al., 435/375, 6, 7.23; 514/44; 536/24.31, 24.32, 24.33, 24.5 :IMAGE AVAILABLE:

10. 5,643,875, Jul. 1, 1997, Human therapeutic uses of bactericidal/permeability increasing (BPI) protein products; Nadav Friedmann, et al., 514/12; 424/85.1, 85.2, 529, 534; 514/21, 921; 530/324, 325, 351, 820 :IMAGE AVAILABLE:

11. 5,641,751, Jun. 24, 1997, Tumor necrosis factor inhibitors; George A. Heavner, 514/13, 12, 14, 15, 16, 17, 18; 530/324, 325, 326, 327, 328, 329, 330 :IMAGE AVAILABLE:

12. 5,632,994, May 27, 1997, Fas associated proteins; John C. Reed, et al., 424/198.1, 185.1, 192.1; 435/7.1, 7.2, 7.9; 530/387.3, 387.9 :IMAGE AVAILABLE:

13. 5,626,843, May 6, 1997, Treatment of autoimmune diseases, including AIDS, by removal of interferons, TNFs and receptors therefor; Simon V. Skurkovich, et al., 424/140.1; 604/6 :IMAGE AVAILABLE:

14. 5,620,889, Apr. 15, 1997, Human anti-Fas IgG1 monoclonal antibodies; David H. Lynch, et al., 435/332; 424/144.1; 435/334, 343.2; 530/387.1, 388.2, 388.23, 388.24, 388.75 :IMAGE AVAILABLE:

15. 5,618,715, Apr. 8, 1997, Oncostatin M and novel compositions having anti-neoplastic activity; Mohammed Shoyab, et al., 435/325, 69.1, 69.4, 320.1, 348, 360, 364, 365.1; 530/300, 351; 536/23.1, 23.51 :IMAGE AVAILABLE:

16. 5,616,491, Apr. 1, 1997, Knockout mice; Tak W. Mak, et al., 435/354, 172.3, 320.1, 355; 536/23.1; 800/2, DIG.1; 935/22, 70 :IMAGE AVAILABLE:

17. 5,610,281, Mar. 11, 1997, Antibodies for modulating heterotypic E-cadherin interactions with human T lymphocytes; Michael B. Brenner, et al., 530/388.85; 424/141.1, 145.1, 154.1, 156.1; 530/387.1, 388.1, 388.22, 388.23, 388.75 :IMAGE AVAILABLE:

18. 5,609,847, Mar. 11, 1997, Treatment methods using metal-binding targeted polypeptide constructs; Benjamin A. Belinka, Jr., et al., 424/1.69, 1.11, 9.1; 530/300, 311; 534/10 :IMAGE AVAILABLE:

19. 5,606,023, Feb. 25, 1997, Mutant tumor necrosis factor proteins; Mann-Jy Chen, et al., 530/351; 424/85.2; 435/69.52 :IMAGE AVAILABLE:

20. 5,605,690, Feb. 25, 1997, Methods of lowering active TNF-.alpha.

levels in mammals using \*\*tumor\*\* \*\*necrosis\*\* \*\*factor\*\*  
\*\*receptor\*\*;  
Cindy A. Jacobs, et al., 424/134.1; 435/69.7; 514/12, 825; 530/350,  
387.3, 866, 868 :IMAGE AVAILABLE:

=> d 20 ab

US PAT NO: 5,605,690 :IMAGE AVAILABLE: L2: 20  
of 70

#### ABSTRACT:

A method for treating TNF-dependent inflammatory diseases in a  
mammal by  
administering a TNF antagonist, such as soluble TNFR.

=> d 20 clms

US PAT NO: 5,605,690 :IMAGE AVAILABLE: L2: 20  
of 70

#### CLAIMS:

##### CLMS(1)

We claim:

1. A method for lowering the levels of active TNF-.alpha. in a  
mammal in  
need thereof which comprises administering to said mammal a TNF-  
lowering  
amount of a TNF antagonist selected from the group consisting of:  
(a) a TNF receptor comprising the sequence of amino acids 3-163 of  
SEQ  
ID NO:1; and  
(b) a chimeric antibody comprising a TNF receptor according to (a)  
fused  
to the constant domain of an immunoglobulin molecule.

##### CLMS(2)

2. A method for lowering the levels of active TNF-.alpha. in a  
mammal in  
need thereof which comprises administering to said mammal a TNF-  
lowering  
amount of a TNF receptor comprising the sequence of amino acids 3-  
163 of  
SEQ ID NO:1.

##### CLMS(3)

3. A method for lowering the levels of active TNF-.alpha. in a  
mammal in  
need thereof which comprises administering to said mammal a TNF-  
lowering  
amount of a chimeric antibody comprising a TNF receptor  
comprising the  
sequence of amino acids 3-163 of SEQ ID NO:1 fused to the  
constant domain  
of an immunoglobulin molecule.

##### CLMS(4)

4. A method for lowering the levels of active TNF-.alpha. in a  
mammal  
having arthritis, which comprises administering to such mammal a  
therapeutically effective amount of a TNF-antagonist selected from  
the  
group consisting of:  
(a) a TNF receptor comprising the sequence of amino acids 3-163 of  
SEQ  
ID NO:1; and

(b) a chimeric antibody comprising a TNF receptor according to (a)  
fused  
to the constant domain of an immunoglobulin molecule.

##### CLMS(5)

5. A method for lowering the levels of active TNF-.alpha. in a  
mammal  
having arthritis, which comprises administering to said mammal a  
TNF-lowering amount of a TNF receptor comprising the sequence of  
amino  
acids 3-163 of SEQ ID NO:1.

##### CLMS(6)

6. A method for lowering the levels of active TNF-.alpha. in a  
mammal  
having arthritis, which comprises administering to said mammal a  
TNF-lowering amount of a chimeric antibody comprising a TNF  
receptor  
comprising the sequence of amino acids 3-163 of SEQ ID NO:1  
fused to the  
constant domain of an immunoglobulin molecule.

=> d 20 fro

US PAT NO: 5,605,690 :IMAGE AVAILABLE: L2: 20  
of 70

DATE ISSUED: Feb. 25, 1997

TITLE: Methods of lowering active TNF-.alpha. levels in  
mammals

using \*\*tumor\*\* \*\*necrosis\*\* \*\*factor\*\* \*\*receptor\*\*

INVENTOR: Cindy A. Jacobs, Seattle, WA

Craig A. Smith, Seattle, WA

ASSIGNEE: Immunex Corporation, Seattle, WA (U.S. corp.)

APPL-NO: 08/385,229

DATE FILED: Feb. 8, 1995

REL-US-DATA: Continuation of Ser. No. 946,236, Sep. 15, 1992,  
abandoned, which is a continuation-in-part of Ser. No.  
523,635, May 10, 1990, Pat. No. 5,395,760, which is a  
continuation-in-part of Ser. No. 421,417, Oct. 13, 1989,  
abandoned, which is a continuation-in-part of Ser. No.  
405,370, Sep. 11, 1989, abandoned, which is a  
continuation-in-part of Ser. No. 403,241, Sep. 5, 1989,  
abandoned.

INT-CL: :6: A61K 39/395; A61K 38/00; C12P 21/04; C07K  
14/715

US-CL-ISSUED: 424/134.1; 435/69.7; 514/12, 825; 530/350,  
387.3, 866, 868

US-CL-CURRENT: 424/134.1; 435/69.7; 514/12, 825; 530/350,  
387.3, 866, 868

SEARCH-FLD: 435/69.1, 69.7, 172.3, 240.27; 424/85.1, 134.1;  
530/351,

387.3, 868; 935/9, 12, 15

#### REF-CITED:

##### U.S. PATENT DOCUMENTS

4,675,285	6/1987	Clark et al.	435/6
4,770,995	9/1988	Rubin et al.	436/544
5,116,964	5/1992	Capon et al.	536/27
5,512,544	4/1996	Wallach et al.	

##### FOREIGN PATENT DOCUMENTS

0308378	6/1989	European Patent Office	C12N 15/00
0422339	7/1990	European Patent Office	C12N 15/12
61-293924	12/1986	Japan	A61K 37/02
0334165	9/1989	Switzerland	C12P 21/00
2218101	11/1989	United Kingdom	C07K 15/14
WO9013575	11/1990	World Intellectual Property Organization	C07K 15/14

# OTHER PUBLICATIONS

Beutler of Tumor Necrosis Factors . . . , Raven Press, 1185 Ave of the Americas, NY, NY, 10036.

Steiner, *Biotechnology* 12: 1313, Dec. 1994.

"US News & World Report", p. 13, Aug. 1, 1994.

*Immunophysiology* pp. 234-235, 1990, Oppenheim.

Pavillo-New Eng J of Med., "Mech. of Disease, Pathogenetic Mech. of

Septic Shock", pp. 1471-1477, 1993.

Hoogenboom et al, *Molecular Immunology* 28(9):1027-1037 1991,

"Construction & Expression of Ab-TNF fusion proteins".

Harris, *The New England Journal of Med.*, 322(18): 1277-1289

(1990)

"Mechanisms of Disease: Rheumatoid Arthritis".

Brennan et al, *The Lancet*, Jul. 29, 1993, 244-247 "Inhib. Effect of

TNF-.alpha. Ab on Synovial Cell IL-1 Production in Rh. Arthritis".

Smith et al, *Science*, 248: 1019-1023, 1990 "A Receptor for TNF

defines an

Unusual Family of Cellular & Viral Proteins".

Bloom, *J. Clin. Invest.*, 91: 1265-1266 (1993) "The Power of

Negative

Thinking".

Pennica et al., "Human tumour necrosis factor: precursor structure,

expression and homology to lymphotoxin," *Nature* 312: 724

(1984).

Gray et al., "Cloning and expression of cDNA for human

lymphotoxin, a

lymphokine with tumour necrosis activity," *Nature* 312: 721

(1984).

Baglioni et al., "Binding of Human Tumor Necrosis Factor to High

Affinity

Receptors on HeLa and Lymphoblastoid Cells Sensitive to Growth

Inhibition," *J. Biol. Chem.* 260:13395 (1985).

Aggarwal et al., "Characterization of receptors for human tumour

necrosis factor and their regulation by .gamma.-interferon," *Nature*

318:665 (1985).

Yoshie et al., "Binding and Crosslinking of .sup.125 I-Labeled

Recombinant Human Tumor Necrosis Factor to Cell Surface

Receptors," *J.*

*Biochem.* 100:531 (1986).

Israel et al., "Binding of Human TNF-.alpha. to High-Affinity Cell

Surface Receptors: Effect of IFN," *Immunology Letters* 12:217

(1986).

Creasley et al., "A high molecular weight component of the human

tumor

necrosis factor receptor is associated with cytotoxicity," *Proc. Natl.*

*Acad. Sci. USA* 84:3293 (1987).

Stauber et al., "Human Tumor Necrosis Factor-.alpha. Receptor," *J.*

*Biol.*

*Chem.* 263:19098 (1988).

Aggarwal and Eessalu, "Induction of Receptors for Tumor Necrosis

Factor-.alpha. by Interferons Is Not a Major Mechanism for Their

Synergistic Cytotoxic Response," *J. Biol. Chem.* 263:10000 (1987).

Tsujimoto et al., "Interferon-.gamma. Enhances Expression of

Cellular

Receptors for Tumor Necrosis Factor," *J. Immun.* 136:2441 (1987).

Holtmann and Wallach, "Down Regulation of the Receptors for

Tumor

Necrosis Factor by Interleukin 1 and 4.beta.-Phorbol-12-Myristate-

13-

Acetate," *J. Immunol.* 139:1161 (1987).

Shalaby et al., "Receptor Binding and Activation of

Polymorphonuclear

Neutrophils by Tumor Necrosis Factor-Alpha," *J. Leukocyte Biol.*

41:196

(1987).

Unglaub et al, "Downregulation of Tumor Necrosis Factor (TNF)

Sensitivity

Via Modulation of TNF Binding Capacity by Protein Kinase C

Activators,"

*J. Exp. Med.* 166:1788 (1987).

Yonehara et al., "A Cell-Killing Monoclonal Antibody (ANTI-Fas) to a Cell

Surface Antigen Co-Downregulated with the Receptor of Tumor

Necrosis

Factor," *J. Exp. Med.* 167:1511 (1988).

Peetre et al., "A tumor necrosis factor binding protein is present in

human biological fluids," *Eur. J. Haematol.* 41:414 (1988).

Seckinger et al., "A Human Inhibitor of Tumor Necrosis Factor

.alpha."

*J. Exp. Med.* 167:1511 (1988).

Seckinger et al., "Purification and Biologic Characterization of a

Specific Tumor Necrosis Factor .alpha. Inhibitor," *J. Biol. Chem.*

264:11966 (1989).

Engelmann et al., "A Tumor Necrosis Factor-binding Protein Purified

to

Homogeneity from Human Urine Protects Cells from Tumor

Necrosis Factor

Toxicity," *J. Biol. Chem.* 264:11974 (1989).

Okayama and Berg, "High-Efficiency Cloning of Full-Length

cDNA," *Mol.*

*Cell. Biol.* 2:161 (1982).

Okayama and Berg, "A cDNA Cloning Vector That Permits

Expression of cDNA

Inserts in Mammalian Cells," *Mol. Cell. Biol.* 3:280 (1983).

Aruffo and Seed, "Molecular cloning of a CD28 cDNA by a high-

efficiency

COS cell expression system," *Proc. Natl. Acad. Sci. USA* 84:8573

(1987).

Yamasaki et al., "Cloning and Expression of the Human Interleukin-

6

(BSF-2/IFN.beta. 2) Receptor," *Science* 241:825 (1988).

Sims et al., "cDNA Expression Cloning of the IL-1 Receptor, a

Member of

the Immunoglobulin Superfamily," *Science* 241:585 (1988).

Tsujimoto et al., *Arch. Biochem. and Biophys.*, "Characterization

and

Affinity Crosslinking of Receptors for Tumor Necrosis" 563-568

(1986).

Suggs et al., "Use of synthetic oligonucleotides as hybridization

probes," *PNAS* 78:6613-6617 (1981).

Kull et al., "Cellular receptor for .sup.125 I-labelled tumor necrosis

factor . . .", *PNAS* 82:5756-5760 (1985).

Smith et al., "A receptor for tumor necrosis factor defines and

unusual

family of cellular and viral proteins", *Science* 248:1019-1023

(1990).

Meller et al., "Complementary DNA cloning of a receptor for tumor

necrosis factor and demonstration of a shed form of the receptor"

*Proc.*

*Natl. Acad. Sci. U.S.*, 87:6151-6155 (1990).

Loetscher et al., "Molecular cloning and expression of the human 55

kd

tumor necrosis factor receptor" *Cell* 61:351-359 (1990).

Schall et al., "Molecular cloning and expression of a receptor for

human

tumor necrosis factor" *Cell* 61:361-370 (1990).

Engelmann et al., "Two tumor necrosis factor-binding proteins

purified

from human urine" *J. Biol. Chem.* 265:1531-1536.

Smith et al., "Blocking of HIV-1 Infectivity by a Soluble, Secreted

Form

of the CD4 Antigen", *Science* 238:1704-1707.

ART-UNIT: 186

PRIM-EXMR: Lila Feisee

ASST-EXMR: John Lucas

LEGAL-REP: Stephen L. Malaska

ABSTRACT:

A method for treating TNF-dependent inflammatory diseases in a

mammal by

administering a TNF antagonist, such as soluble TNFR.  
6 Claims, 7 Drawing Figures

=> d 21-30

21. 5,597,899, Jan. 28, 1997, Tumor necrosis factor muteins; David Banner, et al., 530/351; 435/69.1, 69.5; 530/402 :IMAGE AVAILABLE:

22. 5,593,656, Jan. 14, 1997, Metal-binding targeted polypeptide constructs; Benjamin A. Belinka, Jr., et al., 424/1.69, 9.1, 9.3, 9.4; 530/300, 324, 325, 326, 327, 328, 329, 330; 534/10, 14, 15 :IMAGE AVAILABLE:

23. 5,582,998, Dec. 10, 1996, Monoclonal antibodies against human TNF-binding protein I (TNF-BP I) and immunoassays therefor; G unther Adolf; 435/7.1, 7.92, 7.94, 70.21, 334; 436/811, 815; 530/388.1 :IMAGE AVAILABLE:

24. 5,580,722, Dec. 3, 1996, Methods of determining chemicals that modulate transcriptionally expression of genes associated with cardiovascular disease; J. Gordon Foulkes, et al., 435/6, 91.1, 91.2; 935/77, 78 :IMAGE AVAILABLE:

25. 5,578,461, Nov. 26, 1996, Gene manipulation and expression using genomic elements; Stephen Sherwin, et al., 435/69.1, 172.3, 244, 320.1; 536/23.1, 24.1; 935/28, 33, 55 :IMAGE AVAILABLE:

26. 5,578,288, Nov. 26, 1996, Metal-binding targeted polypeptide constructs; Benjamin A. Belinka, Jr., et al., 424/1.69, 1.11; 530/300, 326, 327, 328; 534/10, 14 :IMAGE AVAILABLE:

27. 5,565,334, Oct. 15, 1996, Enhancer sequence for modulating expression in epithelial cells; Donald Kufe, et al., 435/69.1, 320.1, 371; 536/23.1, 23.2, 24.1, 24.5 :IMAGE AVAILABLE:

28. 5,563,039, Oct. 8, 1996, TNF receptor-associated intracellular signaling proteins and methods of use; David V. Goeddel, et al., 435/7.1, 6, 69.1, 252.3, 320.1; 436/501; 530/300, 350 :IMAGE AVAILABLE:

29. 5,557,032, Sep. 17, 1996, Knockout mice; Tak W. Mak, 800/2; 424/9.2; 435/172.3, 320.1; 800/DIG.1, DIG.4; 935/11, 70 :IMAGE AVAILABLE:

30. 5,543,139, Aug. 6, 1996, 5.5 kD TNF degradation product; John P. Fruehauf, 424/85.1, 520; 530/300, 350, 351, 402, 407 :IMAGE AVAILABLE:

=> d 31-50

31. 5,541,085, Jul. 30, 1996, Method for preparing orphan receptor ligands; Richard D. Holly, et al., 435/69.1, 6, 69.5, 172.3 :IMAGE AVAILABLE:

32. 5,538,863, Jul. 23, 1996, Expression system comprising mutant yeast strain and expression vector encoding synthetic signal peptide; Virginia L. Price, 435/69.1, 254.2, 254.21, 320.1; 536/23.1, 23.4, 23.7, 24.1 :IMAGE AVAILABLE:

33. 5,536,657, Jul. 16, 1996, Recombinant \*\*DNA\*\* encoding human receptor for interleukin-12; Anne O. Chua, et al., 435/252.3, 69.1, 69.52, 320.1; 536/23.5 :IMAGE AVAILABLE:

34. 5,521,295, May 28, 1996, Nucleic acids encoding hybrid receptor molecules; Robert E. Pacifici, et al., 536/23.4; 435/7.1, 172.3, 320.1; 530/350 :IMAGE AVAILABLE:

35. 5,519,000, May 21, 1996, Tumor necrosis factor inhibitors; George A. Heavner, et al., 514/12, 13, 14, 15, 16, 17, 18; 530/324, 326, 328, 329, 330 :IMAGE AVAILABLE:

36. 5,506,340, Apr. 9, 1996, Tumor necrosis factor inhibitors; George A. Heavner, 530/324, 325, 326, 327, 328, 329, 330 :IMAGE AVAILABLE:

37. 5,486,595, Jan. 23, 1996, Tumor necrosis factor inhibitors; George A. Heavner, 530/324, 325, 326, 327, 328, 329, 330 :IMAGE AVAILABLE:

38. 5,486,463, Jan. 23, 1996, TNF-muteins; Werner Lesslauer, et al., 435/69.5, 252.33, 320.1; 530/351; 536/23.5, 23.51 :IMAGE AVAILABLE:

39. 5,478,925, Dec. 26, 1995, Multimers of the soluble forms of TNF receptors, their preparation and pharmaceutical compositions containing them; David Wallach, et al., 530/351; 424/85.1, 158.1, 450 :IMAGE AVAILABLE:

40. 5,470,829, Nov. 28, 1995, Pharmaceutical preparation; Per Prisell, et al., 514/12; 424/85.1; 514/2, 8, 21; 525/54.1 :IMAGE AVAILABLE:

41. 5,470,730, Nov. 28, 1995, Method for producing T.sub.H - independent cytotoxic T lymphocytes; Phillip D. Greenberg, et al., 435/172.3; 424/93.21; 435/69.1, 69.52, 70.4, 252.3, 320.1 :IMAGE AVAILABLE:

42. 5,460,965, Oct. 24, 1995, \*\*DNA\*\* and \*\*RNA\*\* encoding proteins useful in the regulation of KB-containing genes, and cells containing same; Gary J. Nabel, et al., 435/372.3, 172.3, 252.3, 252.33; 536/23.5 :IMAGE AVAILABLE:

43. 5,457,035, Oct. 10, 1995, Cytokine which is a ligand for OX40; Peter R. Baum, et al., 435/69.5, 252.3, 320.1, 364; 530/351; 536/23.5; 935/9 :IMAGE AVAILABLE:

44. 5,455,240, Oct. 3, 1995, Modulators of pneumococcal adhesion to cellular targets involving the platelet activating factor receptor, and uses thereof; Elaine I. Tuomanen, et al., 514/210; 424/122; 514/8, 25; 536/4.1, 17.4, 17.6, 21 :IMAGE AVAILABLE:

45. 5,451,506, Sep. 19, 1995, Oncostatin M and novel compositions having anti-neoplastic activity; Mohammed Shoyab, et al., 435/7.23, 7.1, 7.21, 960; 530/351 :IMAGE AVAILABLE:

46. 5,449,761, Sep. 12, 1995, Metal-binding targeted polypeptide constructs; Benjamin A. Belinka, Jr., et al., 534/10; 530/300, 326, 327, 328, 399, 408; 534/14, 15; 564/18, 23, 26, 27, 28 :IMAGE AVAILABLE:

47. 5,447,851, Sep. 5, 1995, \*\*DNA\*\* encoding a chimeric polypeptide comprising the extracellular domain of TNF receptor fused to IgG, vectors, and host cells; Bruce A. Beutler, et al., 435/69.7, 69.5, 320.1, 328, 365; 530/300, 351; 536/23.4 :IMAGE AVAILABLE:

48. 5,428,012, Jun. 27, 1995, Oncostatin M and novel compositions having anti-neoplastic activity; Mohammed Shoyab, et al., 514/12; 424/85.1, 85.5; 514/21; 530/350 :IMAGE AVAILABLE:

49. 5,422,104, Jun. 6, 1995, TNF-mutins; Walter Fiers, et al., 424/85.1; 435/69.5; 530/351 :IMAGE AVAILABLE:

50. 5,395,760, Mar. 7, 1995, \*\*DNA\*\* encoding \*\*tumor\*\*  
\*\*necrosis\*\*  
\*\*factor\*\*-.alpha. and -.beta. \*\*receptors\*\*; Craig A. Smith, et al., 435/365; 424/85.1; 435/69.4, 172.3; 530/351, 388.23; 536/23.51 :IMAGE AVAILABLE:

=> d 51-70

51. 5,380,747, Jan. 10, 1995, Treatment for atherosclerosis and other cardiovascular and inflammatory diseases; Russell M. Medford, et al., 514/423, 210, 212, 315, 476, 477 :IMAGE AVAILABLE:

52. 5,378,603, Jan. 3, 1995, Method and composition for identifying substances which activate transcription of the LDL receptor gene; Michael S. Brown, et al., 435/6, 4, 29, 172.3; 436/817; 935/76, 79, 82 :IMAGE AVAILABLE:

53. 5,374,423, Dec. 20, 1994, Method of using cytokine receptors on microorganism; Gary R. Klimpel, et al., 424/85.1, 193.1, 197.11, 234.1, 257.1, 258.1, 274.1; 435/252.1, 252.8, 255.4, 849, 879, 922 :IMAGE AVAILABLE:

54. 5,359,039, Oct. 25, 1994, Isolated poxvirus A53R-equivalent tumor necrosis factor antagonists; Craig A. Smith, et al., 530/350; 424/186.1, 232.1; 530/826; 536/23.72; 930/220 :IMAGE AVAILABLE:

55. 5,334,380, Aug. 2, 1994, Anti-endotoxin, interleukin-1  
\*\*receptor\*\*  
antagonist and anti-\*\*tumor\*\* \*\*necrosis\*\* \*\*factor\*\* antibody with arginine-free formulations for the treatment of hypotension; Robert G. Kilbourn, et al., 424/85.2, 145.1, 150.1, 158.1, 164.1; 426/656; 514/12,

21 :IMAGE AVAILABLE:

56. 5,324,818, Jun. 28, 1994, Proteins useful in the regulation of .kappa.B-containing genes; Gary J. Nabel, et al., 530/350; 435/172.3; 935/11, 34, 36 :IMAGE AVAILABLE:

57. 5,270,038, Dec. 14, 1993, \*\*Tumor\*\* \*\*necrosis\*\* \*\*factor\*\*  
\*\*receptors\*\* on microorganisms; Gary R. Klimpel, et al., 424/85.1, 234.1, 257.1, 258.1, 274.1; 435/252.1, 252.8, 255.4, 849, 879, 922 :IMAGE AVAILABLE:

58. 5,256,545, Oct. 26, 1993, Sterol Regulatory Elements; Michael S. Brown, et al., 435/69.1, 172.3, 252.3, 320.1, 358; 536/24.1; 935/36, 43 :IMAGE AVAILABLE:

59. 5,248,671, Sep. 28, 1993, Methods and compositions for treatment of cancer using oligonucleotides; Larry J. Smith, 514/44 :IMAGE AVAILABLE:

60. 5,246,701, Sep. 21, 1993, Method for inhibiting production of IgE by using IL-9 inhibitors; Bernard Dugas, et al., 424/158.1, 85.2, 173.1, 805; 514/8, 21; 530/388.22, 388.23 :IMAGE AVAILABLE:

61. 5,215,910, Jun. 1, 1993, Host cells transformed with sterol regulatory elements; Michael S. Brown, et al., 435/350, 69.1, 172.3, 320.1, 358, 363, 367, 370; 536/24.1 :IMAGE AVAILABLE:

62. 5,135,917, Aug. 4, 1992, Interleukin receptor expression inhibiting antisense oligonucleotides; Ronald M. Burch, 514/44; 530/351; 536/23.5, 24.5 :IMAGE AVAILABLE:

63. 5,135,915, Aug. 4, 1992, Method for the treatment of grafts prior to transplantation using TGF-.beta.; Christine W. Czarniecki, et al., 514/21; 424/85.1; 435/371, 372; 514/12; 530/399; 604/19, 48 :IMAGE AVAILABLE:

64. 5,132,109, Jul. 21, 1992, Method for inhibiting production of IGE and method for enhancing production of IGG using interleukin 9 and inhibitors thereof; Bernard Dugas, et al., 424/85.2, 85.1; 514/8; 530/351 :IMAGE AVAILABLE:

65. 5,087,617, Feb. 11, 1992, Methods and compositions for treatment of cancer using oligonucleotides; Larry J. Smith, 514/44 :IMAGE AVAILABLE:

66. 5,075,236, Dec. 24, 1991, Method of detecting Kawasaki disease using anti-tumor necrosis antibody; Kenji Yone, et al., 436/518; 435/7.1, 7.94; 436/536, 540, 811, 815 :IMAGE AVAILABLE:

67. 4,963,354, Oct. 16, 1990, Use of tumor necrosis factor (TNF) as an adjuvant; H. Michael Shepard, et al., 424/85.1, 85.4; 514/2, 8, 12, 21, 885 :IMAGE AVAILABLE:

68. 4,935,363, Jun. 19, 1990, Sterol regulatory elements; Michael S. Brown, et al., 435/172.3, 41, 212, 226, 375; 536/23.2, 23.5, 23.51, 23.52; 935/6, 34 :IMAGE AVAILABLE:

69. 4,770,995, Sep. 13, 1988, Detection of the sensitivity of cells to the effects of tumor necrosis factor and lymphotoxin; Berish Y. Rubin, et al., 435/7.23; 436/501, 544, 545, 546 :IMAGE AVAILABLE:

70. 4,650,674, Mar. 17, 1987, Synergistic cytotoxic composition; Bharat Aggarwal, et al., 424/85.5, 85.4; 435/69.5; 514/12; 930/143, 144 :IMAGE AVAILABLE: